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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/340,196	06/28/1999	RYOJI KATO	990701	3596

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
10/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/340,196	KATO ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59,68-75,77 and 78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59, 68-75, 77 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. In view of the appeal brief filed on 7/16/2007, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

2. Claims 59, 68-75, 77 and 78 are pending and examined on the merits.

New Grounds of Rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 59, 68-75, 77 and 78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that in the step of determining whether a sample is from a benign thyroid, the comparison rules for making the determination introduce new matter into the specification as originally filed.

The claimed methods require a determination step, where a sample is determined to be malignant if the calculated ratio is either larger or smaller than either the normal or benign standard ratios, and where the sample is determined to be benign in the following case (iii):

(iii) when the calculated ratio is significantly higher than that of the reference fluid sample of the normal thyroid and is significantly lower than that of the reference fluid sample of the malignant thyroid.

In the amendment filed 9/5/2006, this part of the determination step of the claimed methods was introduced, and applicants pointed to Figures 1, 2 and 3 for support for the amendments to the claims. As currently amended, the claims require comparing a calculated ratio to standard ratios for normal thyroid samples and malignant thyroid samples, and the decision is made that a sample is from a benign thyroid if the calculated ratio is significantly higher than that of the reference fluid sample of the normal thyroid and is significantly lower than that of the reference fluid sample of the malignant thyroid

Figure 1 shows a case where the benign ratio is not significantly different from the normal ratio. Therefore, Figure 1 does not support this rule. Figure 2 shows a case where the

benign ratio (for Graves' disease) is significantly smaller than the malignant ratio and significantly smaller than the normal ratio. Therefore, Figure 2 does not support this rule. Figure 3 shows a case where the benign ratio (for follicular adenoma) is significantly higher than both the malignant ratio and the normal ratio, and that the malignant ratio is not significantly different from the normal ratio. Therefore, Figure 3 does not support this rule. Furthermore, examination of Figures 1, 2 and 3, show that per se rules cannot be formed for the entire genus of thyroid disease. For example the data in Figures 1 and 3 conflict with each other, apparently because different sub-types of thyroid malignancies are compared to normal and different types of benign cases. In Figure 1, there is no difference between benign disease (Grave's disease) and normal thyroids, where Con A is the lectin, whereas in Figure 3, where Con A is also the lectin there is a difference between the benign disease ratio (follicular adenoma) and the normal ratio. In both cases, the ratio of thyroglubulin not bound to Con A as a percent is determined. For papillary carcinoma the mean ratio is 4.48, whereas for follicular carcinoma, the mean ratio is 0.83. Therefore, in addition to failing to provide support for the specific case of the rule recited in the claims for comparing a calculated ratio to standard ratios for the determination of whether or not a particular ratio is indicative of benign disease, the specification in general does not appear to provide support the particular rules for determining malignant or benign disease for the entire genus of thyroid malignant disease or the entire genus of malignant benign disease. It is noted that in the originally filed claims, no comparison step was positively recited.

4. Claims 59, 68-75, 77 and 78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods comprising the active steps recited in the

claims of measuring amounts of different types of thyroglubulin based on their differential lectin reactivity, does not reasonably provide enablement for the methods that further comprise steps where comparison rules are used in determining whether a thyroid is malignant or benign as currently recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claimed methods of determining between a malignant thyroid tumor and a benign thyroid tumor require a determination step where calculated ratios are compared to standard ratios. In the case of determining whether a sample is malignant, the calculated ratio must be significantly higher than a reference normal ratio and significantly higher than a reference benign ratio; or the converse must be true that the calculated ratio is significantly lower than each of the two reference ratios. In conflict with this rule for making the determination of whether a sample is malignant or not is the rule set forth in the claims for determining that a sample is benign, where a calculated ratio is determined to be from a benign sample if is significantly lower than a malignant standard ratio and also significantly higher than a normal ratio. Thus, this rule is based on the assumption that a ratio from a benign sample is always less than the malignant ratio

and also always higher than the normal ratio, which is in conflict with applicants' data and is also in conflict with the assumption underlying the rule for determining whether a sample is from a malignant sample. In that rule, the assumption is that the normal ratio may be equal to the benign, less than the benign, or if the ratio is reverse, more than the benign. Therefore, the two comparison rules appear to conflict with each other.

The scope of the claims is very broad because the sample is taken from a living body, with no predetermination of what the possible condition of the patient may have. Furthermore, the malignancy of any type of thyroid cancer is determined using the rules set forth in the determination step, whereas applicants data shows that the ratios vary widely depending on which particular type of thyroid cancer is studied and which lectin is used for determining the amounts of the different types of thyroglublin.

In view of the broad scope of the claims, the logical inconsistency inherent in the statement of the comparison rules set forth for the determination step, and the conflict with applicants' own data, and the fact that applicants' own data demonstrates that malignant ratios vary depending on which type of thyroid malignancy is used as a sample for determining a ratio, the claimed methods as currently recited are not enabled by the specification.

Claim Rejections Withdrawn:

5. The rejection of claims 59, 68, 69, 74 and 77 under 35 U.S.C. 103(a) as being unpatentable over either Nakamura (U.S. Patent 5,571,729; issued 11/5/1996) or Satomura (U.S. Patent 5,780,247; issued 7/14/1998; effective filing 1/5/1991) in view of either Yamamoto (of record), Tarutani (of record), or Survilo (Survilo, L.I. et al., Vestsi Akademii Navuk Belarusi,

Seryya Khimichnykh Navuk, 4: 103-107, 1997; abstract only) is withdrawn because the combination of references does not allow a person of skill in the art to determine whether a sample would be benign as recited in the claims.

6. The rejection of claims 70,71, 77 and 78 under 35 U.S.C. 103(a) as being unpatentable over Katoh (U.S. Patent 5,591,589; issued 1/7/1997) in view of either Yamamoto (of record), Tarutani (of record), or Survilo (Survilo, L.I. et al., Vestsi Akademii Navuk Belarusi, Seryya Khimichnykh Navuk, 4: 103-107, 1997; abstract only) is withdrawn because the combination of references does not allow a person of skill in the art to determine whether a sample would be benign as recited in the claims.

7. The rejection of claims 73 and 77 under 35 U.S.C. 103(a) as being unpatentable over Canfield (WO/87/00289;) in view of Yamamoto (of record) is withdrawn because the combination of references does not allow a person of skill in the art to determine whether a sample would be benign as recited in the claims.

8. The rejection of claims 72, 75 and 77 under 35 U.S.C. 103(a) as being unpatentable over Katoh (supra) in view of Canfield (WO/87/00289;) and further in view of Yamamoto (supra) for the reasons of record is withdrawn because the combination of references does not allow a person of skill in the art to determine whether a sample would be benign as recited in the claims.

Double Patenting

9. The rejection of claims 59, 68, 69, and 74 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 5-9 of U.S. Patent No. 5,780,247 in view of either Yamamoto (of record), Tarutani (of record) or Survilo (Survilo, L.I. et al., Vestsi Akademii Navuk Belarusi, Seryya Khimichnykh Navuk, 4: 103-107, 1997; abstract only) is withdrawn because the combination of references does not allow a person of skill in the art to determine whether a sample would be benign as recited in the claims.

10. The rejection of claims 70, 71 and 78 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 5,591,589 in view of either Yamamoto (of record), Tarutani (of record) or Survilo (Survilo, L.I. et al., Vestsi Akademii Navuk Belarusi, Seryya Khimichnykh Navuk, 4: 103-107, 1997; abstract only) is withdrawn because the combination of references does not allow a person of skill in the art to determine whether a sample would be benign as recited in the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the

status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
October 15, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER